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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/691,383	10/17/2000	Edwin F. Ullman	BEH-7381	3713

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EXAMINER	
COOK, LISA V	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/05/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/691,383	ULLMAN ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group III (claims 19-34) in Paper No. 5 filed 8/29/02 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 5. Currently, claims 19-34 are under consideration.

Priority

3. No benefit of a prior disclosure has been requested in the instant application.

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. For example see page 12. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner-on form PTO-892 or the applicant-on form PTO-1449 have cited the references they have not been considered.

5. The information disclosure statement (IDS) filed 3/6/091 in paper #2 has been considered as to the merits before First Action.

Drawings

6. No drawings were filed in the instant application.

Specification

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. On page 4 of the disclosure a Brief Description of the drawings is included. However, no drawings are in the instant application. Appropriate correction required.

II. The use of the trademarks has been noted in this application. (.i.e. Tween on page 48 line 28). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 19-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 19 is vague and confusing because it is not clear how one drug will be detected simultaneously. It appears that the claim requires at least two or more drugs, therein allowing for the simultaneous measurement of both. Please correct/clarify the intended meaning with respect to simultaneous measurement.

B. Claim 19 steps b and c are vague and indefinite because it is unclear what the first and second reagents comprise. As recited the metes and bounds of the claim cannot be determined. Is it applicant's intent to mean the 1st reagent only comprises a first label and the 2nd regent only comprises a second label? Or will the 1st reagent include a complex of a 1st label-small molecule-drug analogue, while the 2nd reagent includes a complex of the 2nd label-antibody for the small molecule? The claim is further unclear because the interaction of reagents with respect to the drug analog is not clear. How does the drug analog interact/bind/displace binding in the instantly claimed method? Appropriate correction required.

C. Claim 19 step d is unclear in reciting "an increased amount thereof" because it is not certain what reference measurement is being utilized. Is the increased amount in step d to be an increase from the predetermined increased amount of signal in claim 19 step c? In order to obviate this rejection the claim should clearly identify what will constitute an increased amount.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 19-20 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,300,082) in view of Zhang et al. (The Journal of Biological Chemistry, 268 (14), May15, 1993, pages 10095-10101).

Both patents of Erb et al. teach a method and apparatus to measure the binding between a plurality of molecules of a first type to a plurality of molecules of a second type (comprising 1st and 2nd reagents).

The method allows for the direct measurement of binding and dissociation therein evaluating affinity constants, binding constants, binding activity, and complex affinity constants resulting from cooperatively and kinetic parameters for the molecular pair (interaction in close proximity). The method is further taught to be useful in drug design to evaluate their effect through biological receptor binding. See abstract and column 2 lines 20-33. A solution containing a plurality of molecules of interest is combined with a plurality of molecules tagged with absorbance, fluorescence, luminescence, or polarization molecules. The molecular tag may be chemically attached to said plurality of molecules or via an antibody like the claim 19 step (c). Column 15 lines 14-34. In the patent 6,300,082 the molecular tag can be an enzyme, fluorescent, phosphorescent, or luminescent molecule. See claims 8, and 14. Both patents evaluate the signal from the target molecules as an increase over background or control signals (predetermined signals). See '082 column 11 "calibration standard" and '688 column 17 line 35 through column 18 line 23.

Erb et al. and Erb et al. differ from the instant invention in not specifically teaching the simultaneous detection of a plurality of drugs.

However Zhang et al. teach methods of measuring the simultaneous incorporation of two anticancer drugs into DNA. Specifically anthracyclin antibiotics (DAU or DOX) along with an nucleoside analog arabinosylcytosine, which are important anti-cancer drugs are placed with a Dna (sample) molecule thereby allowing for the evaluation of binding with respect to both molecules (DAU or DOX) and the nucleoside analog arabinosylcytosine. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ multiple drugs as taught by Zhang et al. in the drug detection method of Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,300,082) because Zhang et al. taught that DNA is modified by drugs in three ways (intercalation, covalent bound formation, and nucleoside analogue incorporation), and these drug modifications can co-exist in the same DNA molecule without difficulty. "When they [drug modification exhibited by different drugs] occur in close proximity in DNA they may provide an additive inhibitory effect for the target enzyme. In other words increase the drug effectiveness. See abstract. In other words multiple drugs may interact symbiotically in patient systems, therein the evaluation of more than one drug simultaneously would provide information to such an effect.

One of ordinary skill in the art would have been motivated to evaluate multiple drugs in order to extrapolate various data sets for evaluation of drug synergism. See page 10100, Discussion. "Both araC and DAU/DOX are important anticancer drugs that act on DNA. One might imagine that if they occur in close proximity in DNA, as in the present case, they may provide an additive inhibitory effect for the target enzymes".

II. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,300,082) in view of Zhang et al. (The Journal of Biological Chemistry, 268 (14), May15, 1993, pages 10095-10101)and further in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Please see Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,251,688) in view of Zhang et al. as set forth above.

Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,300,082) in view of Zhang et al. differ from the instant invention in not specifically teaching the detection assay employing a solid phase such as particles.

However, Maggio disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186.

Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,300,082) in view of Zhang et al. and Maggio are analogous art because they are from the same field of endeavor, all the inventions teach methods involving immunoassays.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use solid phase/particles as taught by Maggio in the assay method to detection the drugs interaction of Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,300,082) in view of Zhang et al. because Maggio taught that solid phase assay systems employing particles/microplates/discs/tubes/beads "are very convenient to wash thereby reducing labor in assay procedures". Please see page 186.

III. Claims 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,300,082) in view of Zhang et al. (The Journal of Biological Chemistry, 268 (14), May15, 1993, pages 10095-10101) and in further view of Zuk et al. (U.S.Patent#4,281,061).

The teachings of Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,300,082) in view of Zhang et al. are set forth above. However, these references fail to teach the assay as a kit.

Zuk et al. (4,281,061) teach that "as a matter of convenience the reagents [of an immunoassay] can be provided as kits, where the reagents are in predetermined ratios, so as to substantially optimize the sensitivity of the assay in the range of interest" (column 22, lines 63-66).

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay as taught by Erb et al. (US Patent #6,251,688) and Erb et al. (US Patent #6,300,082) in view of Zhang et al. and format them into a kit because Zuk et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay. Although the reference does not specifically disclose that a kit would have instructions which teach how to use said kit, it would have been prima facie obvious to any one of ordinary skill in the art to include instructions which describe how to perform the assay. Applicants should note that the printed matter on the instructions in a kit cannot serve to define the kit over the prior art. See in re Gulack 217 USPQ (CAFC 1983).

10. For reasons aforementioned, no claims are allowed.

Remarks

11. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Lehnen (U.S. Patent #5,567,627) teach methods and reagents useful in the simultaneous and discrete analysis of multiple analytes.

B. Terstappen et al. (U.S. Patent #5,646,001) affinity-binding separation and release of one or more selected subset of biological entities from a mixed population thereof.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
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1/24/03

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PRIMARY EXAMINER
GROUP ~~1800~~ 1641
2/4/03